

# Noninvasive Fibrosis Assessment in Chronic Viral Hepatitis C associated with End Stage Renal Disease

DANIEL COSMIN CARAGEA<sup>1</sup>, BOGDAN SILVIU UNGUREANU<sup>2</sup>,  
DAN NICOLAE FLORESCU<sup>2</sup>, PETRICA POPA<sup>2</sup>,  
MIHAI VICTOR SACERDOTIANU<sup>2</sup>, DAN IONUT GHEONEA<sup>2</sup>,  
CRISTIN CONSTANTIN VERE<sup>2</sup>

<sup>1</sup>Department of Nephrology, University of Medicine and Pharmacy of Craiova

<sup>2</sup>Department of Gastroenterology, University of Medicine and Pharmacy of Craiova

**ABSTRACT:** Introduction. HCV is considered the most encountered viral infection that affect patients after hemodialysis sessions. Even though liver biopsy is considered the golden standard for hepatic diagnosis, additional methods have been used for assessing liver fibrosis. Transient elastography (TE) has evolved as a reference method in some European countries and allows the physician to carry out a fibrosis evaluation in a noninvasive, low-cost and rapid method. Our objective was to assess the efficacy of TE in staging patients with HCV liver disease associated with ESRD, thus choosing the correct moment to perform the procedure. Materials and Methods. We included 34 patients known with ESRD within the regional Nephrology Clinic of Olt County Hospital and also having positive hepatitis C viral liver marker. TE was performed before and hemodialysis and data was analyzed. Results. The patients where we have encountered significant changes were especially within the F0 and F1 stage with a decrease of fibrosis after hemodialysis. Thus, 7 patients which had no fibrosis (F0) went from 4,14±0,98kPa to 3,54±0,84 (p<0,05) and 12 patients from the F1 stage went from 6,22±0,39kPa to 5,47±0,58kPa. The other stages had no significant changes with F2 changing after hemodialysis from 8.03±0,62kPa to 7,76±0,6kPa. Conclusions. TE represents a valuable tool for stiffness assessment and should be taken into considerations as a major option for ESRD patients with liver disease. However, more patients should be enrolled to strengthen this theory and thus providing more reliable results.

**KEYWORDS:** Chronic viral C hepatitis, transient elastography, end stage renal disease

## Introduction

There is an increase rate of viral hepatitis in patients with end stage kidney disease mostly to cross-contaminations in dialysis units. While hepatitis C (HCV) and hepatitis B virus (HBV) are two of the main causes for cirrhosis and hepatocellular carcinoma, there is a continuous need for prevention and therapy to avert disease progression [1].

HCV remains the most encountered viral infection that affect patients after hemodialysis sessions [2].

There is no doubt that most of viral infections that occur in patients with end stage kidney disease are caused by low hygienic measures as well as low adherence of nosocomial transmission.

This implies the need of more attentive follow-up since patients develop a risk for cirrhosis or liver cancer.

Screening for hepatitis in patients with ESRD is done on a regular bases and is based on testing the HCV antibody and HBs surface antigen, and when present an assessment of liver fibrosis is mandatory [3,4].

Even though liver biopsy is considered the golden standard for hepatic diagnosis, additional methods have been used for assessing liver fibrosis [5].

Transient elastography (TE) has evolved as a reference method in some European countries and allows the physician to carry out a fibrosis evaluation in a noninvasive, low-cost and rapid method [6-9].

Thus, this is a new alternative for the patient, which offers a pain-free assessment and avoids possible induced complications. However, there are some situations where TE is not very accurate, especially in acute liver disease or right heart failure which might be caused by liver congestion.

Our aim was to assess the efficacy of TE in staging patients with HCV liver disease associated with ESRD, thus choosing the correct moment to perform the procedure.

## Patients and Methods

We included 34 patients known with ESRD within the regional Nephrology Clinic of Olt County Hospital and also having positive hepatitis C viral liver marker.

We followed only patients with positive antibodies for hepatitis C which agreed to participate in this study by signing an informed consent.

We defined hemodialysis patients with a creatinine clearance less than 15ml/min per 1.73m of body surface which had a 3 week dialysis for more than 2 years.

We did not include patients that associated other liver disease situations such as autoimmune hepatitis or positive serology for hepatitis B, primary biliary cirrhosis, alcohol consumption or decompensated cirrhosis.

All demographic data and routine biological analysis were included for each patient such as hemoglobin, white blood cell count, platelet count, ALT, AST, albumin, total bilirubin, which also helped provide a better assessment for the liver disease.

Abdominal ultrasound was performed for each person and helped exclude patients with other pathologies or with advanced liver disease.

We also focused on measuring the spleen diameter before and after hemodialysis.

Liver Fibrosis was measured by using the Fibroscan device (EchoSens, Paris, France), according to the National Romanian guidelines on elastography published in 2014.

The procedures were performed by a single experienced operator within the Gastroenterology Clinic of the University of Medicine and Pharmacy of Craiova, Romania and were selected patients on which was used only the standard M transducer with a 3.5MHz.

Tissue stiffness was related into kilopascals and the patients were staged in fibrosis stages.

Measurements were performed for each patient in supine position with the right arm over the head to allow the probe to have a better access to the liver's right lobe. Ten consecutive measurements were taken into account with the IQR with a success rate of over 60%.

We used as reference the stiffness assessment provided by De Ledinghen and Vergniol [10] which sets the standard as follows: F0<5.4kPa, F1=5.5-6.9kPa, F2=7-9.4, F3=9.5-14.4, F4>14.5.

We decided to consider significant fibrosis with threshold above 7kPa. Two measurements were performed with overnight fasting just before hemodialysis and after the procedure to see how these settings might influence the results. All measured were statistically analyzed using SPSS (Chicago IL, America).

The duration and the amount of fluid removal in each patient was measured within the dialysis session.

## Results

The characteristics of the 34 patients with chronic viral C hepatitis were analyzed.

While the etiology of the ESRD was not taken into account, we only followed the baseline characteristics as well as the laboratory findings from each patient.

Thus, 20 patients were male with a mean age of 51±14 years and 14 were female with a mean age of 44±16 years.

Most of the patients came from the country side, and most of them had diabetic nephropathy, hypertensive nephrosclerosis and chronic interstitial nephritis kidney disease.

There was also a significant number of patients who were having blood transfusions, with 17 patients having received more than 5 units of blood.

The duration of the hemodialysis for the 34 patients was 3.76 h and the median amount of fluid removed within the session was 2.32 (Table 1).

**Table 1. Patients' characteristics, ESRD etiology and laboratory findings among the 34 selected patients for fibrosis assessment**

Patients' Characteristics	n=34
Age (men)	51±14
Age (women)	44±16
BMI (kg/m <sup>2</sup> )	21.3±4.1
ESRD Duration	3.76±1.3
ESRD fluid removal	2.32±0.9
<b>ESRD etiology</b>	
Diabetic nephropathy	23.3 %
Hypertension nephropathy	28.4 %
Chronic interstitial nephritis	31.5 %
Other	16,8%
<b>Laboratory Analysis</b>	
Hemoglobin g/dl	9,4±1,2
White blood cells (mmc)	6543±1400
Platelets (mmc)	212.000±54320
AST (ULN)	45.3±16.23
ALT (ULN)	52.17±13.14
Total Bilirubin (mg/dl)	0.81 ±0.3
Albumin (g/dl)	3,5±0,8
Creatinine (mg/dl)	7,4±2,4
<b>INR</b>	<b>1,3±0,5</b>

Fibrosis was assessed by TE in each patient before and after dialysis. Changes were observed in liver stiffness measurements (kPa) and body weight in each patient after TE session.

Most of the patients had a low level of fibrosis. From the 34 patients, we encountered 7 with F0 fibrosis score, 12 patients with F1

fibrosis score and 6 patients with F2 fibrosis score.

There was a lower number of patients with a high level of fibrosis with 4 patients found with F3 and 5 patients with F4.

We observed that the 34 patients had a fibrosis with a mean value of 11.53kPa, regardless the fibrosis stage and after the dialysis session we observed a minimal decrease to 10.21kPa.

There was also a change in body weight with a decrease of nearly 1.43kg after hemodialysis.

The patients where we have encountered significant changes were especially within the F0 and F1 stage with a decrease of fibrosis after hemodialysis.

Thus, 7 patients which had no fibrosis (F0) went from  $4,14 \pm 0,98$  kPa to  $3,54 \pm 0,84$  ( $p < 0,05$ ) and 12 patients from the F1 stage went from  $6,22 \pm 0,39$  kPa to  $5,47 \pm 0,58$  kPa.

The other stages had no significant changes with F2 changing after hemodialysis from  $8,03 \pm 0,62$  kPa to  $7,76 \pm 0,6$  kPa, F3 from  $10,9 \pm 1,08$  to  $10,82 \pm 1,02$  kPa and F4 from  $28,36 \pm 4,07$  to  $28,48 \pm 4,02$  kPa (Fig.1, Table 2).

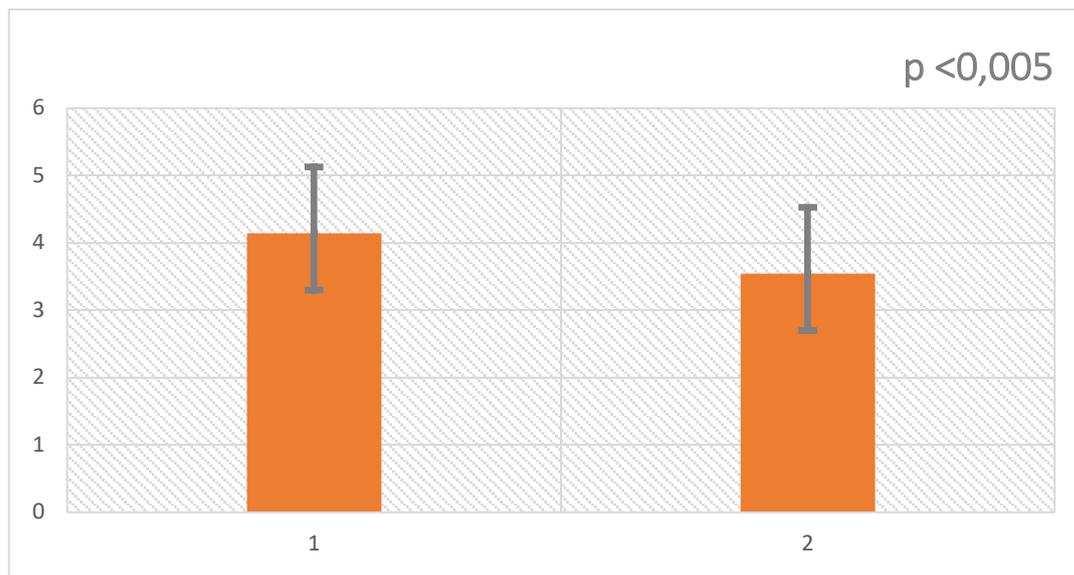


Fig.1. F0 fibrosis showing the difference encountered stage before (1) and after dialysis (2)

Table 2. Fibrosis assessment results using TE in patients just before hemodialysis and after dialysis

Fibrosis Stage	Fibroscan before hemodialysis (kPa)	Fibroscan after hemodialysis (kPa)	p value
F0	$4,14 \pm 0,98$	$3,54 \pm 0,84$	0,005
F1	$6,22 \pm 0,39$	$5,47 \pm 0,58$	0,001
F2	$8,03 \pm 0,62$	$7,76 \pm 0,6$	0,046
F3	$10,9 \pm 1,08$	$10,82 \pm 1,02$	0,259
F4	$28,36 \pm 4,07$	$28,48 \pm 4,02$	0,141

## Discussions

Hepatitis C infection in patients following dialysis is a well-known problem that still requires extensive attention. Several conditions have proven to affect liver fibrosis assessment such as cholestatic disease, acute hepatitis, the presence of ascites, heart failure and dialysis [11-15].

Our study highlighted that patients with ESRD had different values of fibrosis measured through a non-invasive technique, with changes before and after the procedure. Our study proves that hemodialysis may influence the fibrosis that

we encounter after TE especially in low fibrosis scores of F0-F2.

Chronic liver injury leads to fibrosis and further on to cirrhosis and hepatocellular carcinoma. Preventing this continuous process by eliminating the aggressive factors during the fibrosis stages may help interrupt the disease evolution. Thus a rapid assessment provides a better reflection on what therapy should be more indicated in patients with chronic liver disease. Hepatitis C infection assessment on liver fibrosis with TE has successfully replaced the need of liver biopsy and proved to be a reliable tool due to easy handling and precise results. However,

TE should be performed on a certain protocol as it may be influenced by several conditions, especially hepatic congestion [13,14].

Patients with hemodialysis are more exposed to hepatitis C infection than the general population due to nosocomial transmission or rather low hygienic measures. Also it seems that this process may influence the TE results and the fibrosis assessment should be performed under controlled situations due to a state of fluid that may cause liver congestion. Our study revealed that TE may have different results before and after dialysis, and the right moment to perform this procedure should be after fluid withdrawal. While similar studies have been performed on other situations that may cause hepatic congestion, we proved that the better way to assess fibrosis in HCV ESRD association is just after hemodialysis. Decompensated right heart failure and the use of diuretics have also shown different values after TE, thus highlighting different fibrosis stages when used [15].

Our results showed that the major changes were in patients with a low level of liver fibrosis from F0 to F2 rather than patients with advanced disease. We observed that some patients had no underlying liver disease, but only the HCV infection, thus just after hemodialysis the TE results showed lower values. This might be due to fluid overload in ESRD and after a fluid removal of more than 2.5 L a significant decrease of TE level was encountered. However, along with increase in fibrosis score, especially F3 and F4 we did not observed similar results which might be due to a preexisting liver disease. There seems to be a threshold where ESRD stops influencing TE values which correlates with disease progression.

There are a number of studies that focused on similar situations [17-20].

We have obtained rather similar results with the existing data, even though there are some studies that suggested that along with disease progression after a value of 10kPa, the proper moment to assess the liver disease is after hemodialysis as it may increase liver fibrosis [21].

Our results are backed up by Taneja et al. [16] which after analyzing 68 patients with HCV infection and ESRD confirmed that TE may have different results and this procedure should be performed under precise conditions. They concluded that after a single ESRD session, TE should be immediately performed due to fluid withdrawal, thus ensuring a better diagnosis of existing fibrosis. The timing of TE in ESRD

patients seems to be the most important factor, especially in patients with a fibrosis score lower than 7kPa.

Our major drawback was the fact we only assessed the patients using TE and did not use the METAVIR score for fibrosis evaluation after liver biopsy. Even though we have enrolled 34 patients with HCV infection, our study might be a relevant contribution to this limited field which has been receiving extensive attention along with therapies of hepatitis C.

## Conclusion

TE represents a valuable tool for stiffness assessment and should be taken into considerations as a major option for ESRD patients with liver disease.

With no major risks, the timing of the procedure seems to be significant factor, which may help differentiate between patients with fibrosis and the ones with liver congestion, where fibrosis might actually be even ruled out.

However, more patients should be enrolled to strengthen this theory and thus providing more reliable results.

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**Correspondence Author: Bogdan Silviu Ungureanu, Department of Gastroenterology,  
University of Medicine and Pharmacy of Craiova, Adress: 66, 1 Mai Blvd, 200638 Craiova, Romania,  
e-mail: bogdan.ungureanu@umfvcv**